EXPERIMENTS WITH COCAINE PHENATE AS A LOCAL ANESTHETIC.

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So much has been written of late concerning the deleterious systemic effects of cocaine hydrochlorate when used topically upon the mucous membrane or injected by means of the hypodermatic syringe, especially in patients who have organic lesions of the heart or kidneys, that we hesitate to employ it in many cases for fear there may be some idiosyncrasy and that the full physiologic action of the drug may be manifested.

Alarming symptoms often arise from its use, and one often wishes for a drug that would give us the local anesthesia without the probability of the systemic effect.

At the present time it is next to impossible to treat successfully diseases of the eye, nares, pharynx and larynx, or to perform operations upon these parts, without the aid of cocaine; therefore, the manufacturing chemist has been trying to produce some preparation that would possess the advantages without the disadvantages.

On account of the great similarity between the local effects of cocaine and those of phenol, both

agents causing local anemia and anesthesia, and because it had been proposed to make extemporaneous mixtures of the two drugs to lessen the systemic effect of the former, it occured to Von Oefele [1] to combine the two substances in such a way as to form a salt perhaps, would have the anesthetic action of both, with the slow-absorbing power of the latter.

In cocaine phenate I believe we have this desired result. It is prepared by Merck, and his description [2] is as follows: "It is a slightly colored substance of *thick-honey consistency*, which readily melts when heated, and whose percentage of cocaine alkaloid is 75. It is readily soluble in a 50 per cent. solution of alcohol. The solution has a faint odor of carbolic acid."

It is extremely deliquescent, my attention having been directed to this quality by my friend Mr. Swartley, who prepared the various solutions for me; it is also soluble in albolene, one of the bland oils produced from the coal-tar group. The dose is from gr. $\frac{1}{12}$ to gr. $\frac{1}{6}$ by the stomach. Locally, "it coagulates the albumin in the tissue, preventing the absorption of the cocaine, thereby prolonging the anesthetic effect and lessening the danger of systemic poisoning." [3]

In this combination, therefore, we possess, theoretically, a drug which has local anesthetic properties with slow-absorbing power, and which should also be slightly antiseptic.

Determining to test for myself the properties of

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[1] Merck's Bulletin, June, 1891, p. 77.

[2] Ibid., February, 1890, p. 10.

[3] Hare: Therapeutic Gazette, January, 1893, p. 19.

the drug as far as the effect upon mucous membranes was concerned, I had prepared alcoholic solutions and solutions in albolene.

My first experiment was upon my own eye.

THE EYE.—On the lower lid of my left eye I placed one drop of the alcoholic solution of 4 per cent. strength, and, as anticipated, experienced a severe burning pain compelling me to close the lids immediately. Upon opening them there was found intense hyperemia of the conjunctiva, lachrymation, and slight photophobia.

In two minutes another drop was placed on the same lower lid, and the symptoms were similar, though not so severe. In four minutes from the time the first drop was instilled there was anesthesia of the conjunctiva of the lower lid, of the lower half of the cornea, and of the corresponding ocular conjunctiva—these being the parts with which the substance had come in contact. The anesthesia lasted for six minutes, and then gradually disappeared. The pupil was very slightly dilated. There were muscular twitchings in the lower lid similar to those caused by an instillation of a solution of eserine, but not so severe or so prolonged in action.

On the lower lid of the other eye the experiment was repeated with a 4 per cent. solution of the drug in albolene. When the the first drop was instilled there was a slight stinging sensation which caused me to close the lids, but lasting for an instant only. The conjunctiva was found to be paler than before the instillation. There was no lachrymation, and no photophobia. In two minutes another drop was placed upon the conjunctiva, and the immediate

effect was barely noticeable. In five minutes after the first instillation the conjunctiva of the lower lid and of the lower half of the eyeball was more anemic than before the experiment, and, in addition, the lower half of the cornea was anesthetized so thoroughly that pledgets of absorbent cotton and tissue paper could be rubbed against the parts without producing any sensation whatever. Sensation did not begin to return until ten minutes from the time its absence was first noticed, or fifteen minutes from the beginning of the use of the solution.

The pupil was widely dilated and gradually increased in size for about forty-five minutes, when it had reached the maximum. It was not reduced to the size of its fellow until the following day, though the experiment was conducted early in the morning.

There was no paralysis of accommodation in either eye, but the "range" was changed, the near point being carried farther from the eye—in the eye upon which the last experiment was conducted it being about four inches in front of the original near point. My distant vision was slightly impaired, the letters appearing somewhat hazy, though I could still read 20/XX with very little difficulty.

The palpebral fissure was not appreciably enlarged in either eye, and there was no ptosis. The same character of twitching of the muscles of the lower lid was observed as in the other eye.

On the following day, I endeavored to ascertain whether, in the last experiment, it was the cocaine phenate or the albolene that produced the slight burning sensation when first introduced, and for this purpose placed a drop of albolene on the same

part of the conjunctiva that, on the preceding day, had been touched by the solution of cocaine phenate in albolene. The result was entirely negative; there was no greater sensation than if a drop of distilled water had been used; thus proving to me that it was the cocaine phenate that caused the peculiar burning sensation when the solution in albolene was introduced, and that this solution had given me the true effect of the drug upon the eye.

The Mouth.—With a 4 per cent. solution I brushed the right half of my tongue from the tip as far back as I could well reach. In from two to three minutes the anesthetic action had begun; there was decided numbness of this side. In five minutes the application was repeated, the tongue being held out of the mouth as long as possible, to prevent the saliva from washing the solution away. In five minutes more—ten minutes from the beginning of the experiment—the right side of the tongue was so numb that an instrument drawn over it could not be felt. I then scratched my tongue on the right side with a pointed instrument, and, though the procedure was appreciated, it gave me no pain, as did the same procedure upon the opposite side. Next, I touched the right side of my tongue, at different times, with solutions of sugar and strychnine, but could not perceive the taste, though easily recognized on the left side. The numbness had disappeared and the taste returned in twenty minutes from the first application.

At another time I painted my lips and my gums, and the same anesthetic effect was produced, which

reached the maximum in about ten minutes, and had entirely disappeared in twenty minutes.

THE NARES.—In the nares I sprayed some of a 4 per cent. solution in alcohol, and the anesthetic effect was more marked than on the mucous membrane of the mouth. At first there was a stinging sensation, similar to that produced in the conjunctiva, which I attributed, for the most part, to the alcohol in the solution, as spraying the other side of the nose with a solution in albolene, of the same percentage, did not cause more than a momentary burning sensation. The anesthetic effect of the latter solution came on a little later than that of the former, though, as far as could be judged, it reached the same degree of intensity. With the first solution the parts were benumbed almost from the first, the loss of sensation reaching a maximum in about eight minutes, and disappearing entirely in about fifteen minutes. By thoroughly spraying my nasal cavity with my head in such a position as to allow the solution to come in contact with the upper parts, where the terminal filaments of the olfactory nerve are situated, I was able to impair, but not to destroy, the sense of smell. This was destroyed at another time by the use of an 8 per cent. solution, and returned in eight minutes after it had disappeared.

THE LARYNX AND TRACHEA.—In my own larynx and trachea I was unable to test the effect of the drug, but this was done upon two of my patients, the larynx of one being tuberculous, that of the other being perfectly healthy. In the former, the use of a spray of a 4 per cent. solution of

cocaine hydrochlorate, in the larynx and trachea always caused giddiness, slight nausea, nervousness, and insomnia, which lasted during the day and night following the application. Upon spraying this patient's larynx with a 4 per cent. solution of cocaine phenate, I could not produce as great an anesthetic effect as with the hydrochlorate, so I increased the percentage, employing a 6 per cent. and then an 8 per cent. solution. The 6 per cent. solution of the phenate caused about the same effect as the 4 per cent. solution of the hydrochlorate, but the anesthesia, as far as I could judge, lasted a little longer from the use of the former drug. With the aid of this solution I was able to make applications to the tuberculous ulcers in about eight minutes after spraying the larynx.

In the larynx of the healthy patient, the anesthesia was produced in about the same time. In neither case was it possible to say when the effect had entirely disappeared.

While intra-laryngeal medication was facilitated by the use of cocaine phenate, spasm was not prevented, and in this respect the action is similar to that of the hydrochlorate.[1]

THE URETHRA.—Through the courtesy of one of my surgical friends, I made some observations in the case of a patient in which bougies were being employed for the gradual dilatation of a stricture of the urethra, the canal being so extremely sensitive that at times the bougies could be passed but a short distance beyond the meatus.

I introduced a dram of a 4 per cent. solution

[1] J. M. Da Costa, THE MEDICAL NEWS, December 13, 1884.

of cocaine phenate in albolene into the urethra, holding it there for five minutes, when a No. 30 steel bougie (French scale) was passed without any difficulty, the patient's statement being that he could "feel something," but that was all.

THE EAR.—For the sake of making my experiments complete, I regret that I have not had an opportunity, since using the drug, to perform some operation on the ear under the anesthesia produced by it. Suffice it to say that no difference could be distinguished between its action and that of the hydrochlorate, when a drop was placed in the external auditory canal.

Reports of the successful use of cocaine phenate hypodermatically have been published by Vian[1] and by Kyle,[2] though Von Oefele states that he has not yet found a suitable solvent for this mode of administration, the alcoholic solution which he used causing severe pain. I have not had any opportunity to try the albolene solution in this manner, though I believe it will be less painful than the alcoholic.

The one quality in particular that has been claimed for cocaine phenate is that it produces the local anesthetic effect, without any systemic effect; so it is to be hoped that those members of the profession who have patients presenting an idiosyncrasy to the local use of the hydrochlorate will give the phenate a trial, and report the results.

My employment of the drug beyond experimental purposes has been confined to the treatment of diseases of the eye, ear, throat, and nose.

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[1] Nouveaux Remèdes, 1887, p. 192.

[2] Therapeutic Gazette, January, 1893, p. 18.

The following are the reports of some cases in which the drug was used:

Case I.—Male, aged forty-one years, of tuberculous family history; was referred to me by a medical friend for treatment of a constant hacking cough, there being no change in the pulmonary signs from the normal. Upon examination, laryngeal tuberculosis was found, accompanied by some ulceration. The man was immediately placed upon the customary treatment; but upon receiving the spray of cocaine hydrochlorate, of 4 per cent. strength, prior to the intra-laryngeal applications, he always became dizzy, nervous, irritable, and could not sleep well during the night which followed. This occurred after every application. When a solution of cocaine phenate, of 5 per cent. strength, was substituted, none of the symptoms noted was present, and the patient noticed the marked difference at once. The latter solution has been in use on this patient for some time, and there has not yet been noticed the slightest systemic effect.

Case II.—Male, aged thirty-eight years, with a tuberculous history, came for the treatment of harassing cough and irritable throat, which had existed ever since patient had had influenza, ten months before. Examination showed extensive ulceration of the right vocal band, tuberculous in character, and a beginning laryngeal tuberculosis. Using a solution of cocaine hydrochlorate of 5 per cent. strength, I anesthetized the band and surrounding parts as thoroughly as possible prior to using the curette, and while performing the operation, symptoms similar to those displayed in the preceding case, but much more severe, supervened. After this, whenever the throat was sprayed with cocaine hydrochlorate, slight nausea, vertigo, and insomnia followed. A 6 per cent. solution of the phenate was

substituted, and there have been no unpleasant symptoms since, though I use it two or three times a week for making applications, and have thoroughly anesthetized the parts twice with it for the purpose of curetting the ulcer.

Case III.—A female, aged twenty-two years, of good history, presented herself for treatment of the throat, which she was constantly "clearing." I found large follicles in the pharynx, on which I used the galvano-cautery, having first sprayed the throat with a 4 per cent. solution of cocaine phenate. The result was fully as satisfactory as in the cases in which the hydrochlorate had been used.

Case IV.—A male, aged twenty-six, had chronic hypertrophic rhinitis. I found a large inferior turbinated bone almost occluding the right nasal cavity which, without any difficulty, was removed by the aid of a 6 per cent. solution of cocaine phenate.

Case V.—A male, aged forty-two, had had a foreign body in cornea for twenty-four hours. There had been unsuccessful attempts at removal. I instilled three drops of a 4 per cent. solution of cocaine phenate, and removed the particle with my spud, very easily and without pain. The drug also seemed beneficial in breaking up the conjunctivitis which was necessarily present.

Case VI.—A female, aged twenty-eight, with an ulcer of the cornea of six weeks' duration. After using two drops of a solution of cocaine phenate of 5 per cent. strength, which was repeated in five minutes, I was able in ten minutes from the first instillation to cauterize the ulcer with the actual cautery without the patient suffering any pain.

Case VII.—A male, aged ten, with convergent strabismus. I instilled a solution of cocaine phenate of 6 per cent. strength, and divided the internal

rectus of the right eye with as little pain as is experienced when the hydrochlorate is used.

Though the cases cited are few in number, the drug has been used by me in many others with equally good results. From the foregoing experiments and cases it seems that the following conclusions are justifiable:

1. In cocaine phenate we have a drug that can be successfully used, without producing systemic effects, in those cases in which there exists an idiosyncrasy to the local use of cocaine hydrochlorate.

2. As good an anesthetic effect can be produced with cocaine phenate as with cocaine hydrochlorate, but stronger solutions are required to produce the same degree of anesthesia.

3. The anesthesia does not come on so quickly with the phenate as with the hydrochlorate, but lasts fully as long, if not longer, than the anesthesia from the latter.

4. In some cases, though there be no physiologic contra-indication to the use of the hydrochlorate, the phenate is to be preferred on account of its antiseptic properties.

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